REMARKS

Claims 43 and 44 have been cancelled without prejudice or disclaimer. New claims 45-47 have been added. No new matter has been added by virtue of the within amendments. For example, support for new claims 45-47 can be found throughout the specification and in the original claims of the application. In particular, new claims 45 and 46 are presented merely to recite the subject matter of claims 43 and 44 in independent form; support for new claim 47 appears in claim 42.

Applicants appreciate the indication of allowable subject matter, i.e., that claims 33 to 38 are allowed, that claim 39 would be allowable but for an informality, and that claims 43 and 44 would be allowed if presented in independent form.

As an initial matter, Applicants note that claim 39 has been amended as suggested in the Office Action to recite a proper multiple dependency. Additionally, Applicants have rewritten the subject matter of claims 43 and 44 in independent form as new claims 45 and 46. Newly added claim 47 depends from claim 45. Thus, it is believed that each of claims 39 and 45-47 should be allowed.

Referring now to the only outstanding rejection, claims 40-42 stand rejected under 35 USC §112, 1st paragraph. As the rejection is understood, the position is maintained that the treatment of all cancerous cells by any one compound is allegedly not enabled by the present application.

The rejection is traversed.

Apoptosis is a cell suicide mechanism invoked in disparate situations, both physiological and pathological, to ablate unwanted, damaged, or potentially neoplastic cells. Applicants have surprisingly discovered that the PBR ligands described in the present application induce apoptosis in **9 cell lines**, namely Jurkat (leukemic T cell lymphoblast

cells), HL-60 (promyelocytic leukemia cells), Hut-78 (T-cell leukemia), LAMA, KYO.1 and K562 cells which are all CML (chronic myeloid lymphoma) cells, CEM (T lymphoblastoid) cells, HeLa (cervix carcinoma) cells and MCF-7 (human breast carcinoma) cells.

The Office Action cites case law where evidence involving a single compound and two types of cancer was held insufficient to establish the utility of claims directed to a method of treating two cancers. As noted above, Applicants have presented evidence relating to **9 cell lines**.

Moreover, attention is directed to Table 2 of the application. Table 2 illustrates the effect of PBOX compounds on apoptosis in HL-60 cells. For example, PBOX 6 is found to induce 38.6 ± 4.6% apoptosis in HL-60 cells. Applicants offer the enclosed further table of results which demonstrate the ability of the claimed compounds to induce apoptosis in additional cell lines such as prostate cancer (PC3) and ovarian carcinoma (OAW42), for example. The enclosed table is for information purposes and is provided in support of Applicants' argument that claims 40-42 are fully enabled. For example, the table shows that treatment of prostate cancer cells (PC3) with 10μM PBOX 6 for 16 hours (i.e., similar conditions to those used in Table 2 of the present application) induced 39% apoptosis. Applicants would be pleased to provide a Declaration in connection with the enclosed data should it be required.

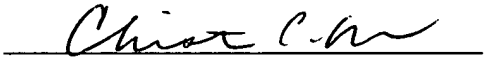
In further support of Applicants' position, enclosed is a paper entitled "Tumor selective G_2/M cell cycle arrest and apoptosis of epithelial and hematological malignancies by BBL22, a benzazepine" (Xia et al., *PNAS*, June 20, 2000, vol. 97, no. 13, pp. 7494-7499). This paper describes a PBR ligand, BBL22, which induces arrest in the G_2/M phase of the cell cycles in human tumor cell lines of both epithelial and hematopoietic cellular origin. In particular, this reference teaches that several tumor types, notably prostate and certain breast cancer cell lines, exhibit significant apoptosis when treated with BBL22.

In view of the foregoing, it follows that the skilled artisan would readily understand that the present invention describes and is indicative of how the claimed compounds would behave in the body. As such, the full scope of claims 40-42 is enabled. In summary, it is submitted that the present application together with the knowledge possessed by one skilled in the art provide ample enablement for claims 40-42.

Reconsideration and withdrawal of the rejection are thus requested.

It is believed the application is in condition for immediate allowance, which action is earnestly solicited.

Respectfully submitted,



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VERSION MARKED TO SHOW CHANGES

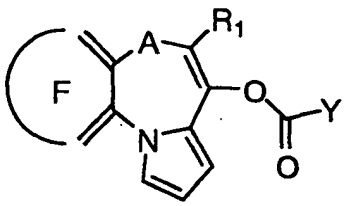
IN THE CLAIMS:

Claim 39 was amended as follows:

39. A pharmaceutical composition comprising the compound of any one of claims 33-38 and a pharmaceutically acceptable carrier.

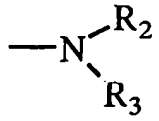
The following new claims were added:

45. A method for selective apoptosis in cancerous cell lines selected from the group consisting of leukemic T cell lymphoblast cells (Jurkat), promyelocytic leukemia cells (HL-60), T-cell leukemia cells (Hut-78), chronic myeloid lymphoma cells (CML), T lymphoblastoid cells (CEM), cervix carcinoma cells (HeLa) and human breast carcinoma cells (MCF-7), comprising:
administering to a subject in need thereof, a pharmaceutically effective amount of a compound of formula I



wherein:
(i) R_1 represents an unsubstituted C_6 or C_{10} aryl group; or a C_6 aryl group substituted with Me or OMe;
(ii) A represents O, S; or a sulfur atom oxidized to sulfoxide;
(iii) the cyclic group labeled F represents an unsubstituted C_6 or C_{10} aryl or a C_5 heteroaryl group having nitrogen as a heteroatom or a phenyl group substituted with ethoxycarbonyl function; and

(iv) Y represents the group



wherein R_2 and R_3 are independently hydrogen; or methyl or ethyl;
or Y represents the group CH_3; or $(CH_2)_2CH_3$ or an unsubstituted C_5 heteroaryl group having nitrogen as a heteroatom; and
assessing the affects of the administration.

46. The method of claim 45 wherein the chronic myeloid lymphoma cells are selected from the group consisting of LAMA, KYO.1 and K562 cell lines.

47. The method of claim 45 wherein the subject is a human or animal.